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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/671,658	09/27/2000	Daniel M. Gorman	15631-005920US	5950

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EXAMINER

JAMROZ, MARGARET E

ART UNIT	PAPER NUMBER
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1644

DATE MAILED: 01/29/2002

13

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/671,658

Applicant(s)

GORMAN ET AL.

Examiner

Margaret E Jamroz

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 25 October 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-10 is/are pending in the application.
- 4a) Of the above claim(s) 4 and 5 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-3 and 6-10 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4 and 11.
- 4) ☐ Interview Summary (PTO-413) Paper No(s) \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☒ Other: *notice to comply and CRF report*.

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#### DETAILED ACTION

1. Claims 1-10 are pending.

Applicant's election with traverse of Group II (claims 1-3 and 5-10) in Paper No. 9 is acknowledged. The traversal is on the ground(s) that antibodies and anti-idiotypic antibodies do not differ with respect to their structure and mode of action. This is not found persuasive antibodies bind to antigens while anti-idiotypic antibodies bind to antibodies; further, they have acquired a separate status in the art as shown by different classification and/or recognized divergent subject matter.

The requirement is still deemed proper and is therefore made FINAL.

Applicant further elects species of antagonistic antibodies. Claims 1-3 and 6-10 read on the elected species.

Claim 4 (non-elected group I) and claim 5 (non-elected species of Groups II) are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to a non-elected inventions.

Claims 1-3 and 6-10, wherein the antibody specifically binds to a 499E9 polypeptide comprising SEQ ID NO: 2 and is antagonistic are under consideration in the instant application.

2. The specification on page 1 should be amended to indicate that the instant application claims priority under 35 U.S.C. 120 to application 08/989,362, now patent 6,242,586.
3. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention *to which the claims are directed*.
4. Claim 10(b) is objected to because of the following informalities: "4999E9" should be "499E9". Appropriate correction is required.

#### ***Claim Rejections - 35 USC § 112***

5. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-3 and 6-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
7. The term "binding fragment" in claims 1-10 is a relative term which renders the claim indefinite. The term "binding fragment" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is suggested that the claim recite "antigen binding fragment".

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8. The term "antibody binding fragment" in claim 7 is a relative term which renders the claim indefinite. The binding fragment is an antibody which binds to a protein/peptide and can be a fragment. It is suggested that the claim recite "antigen binding fragment".

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claim 10 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for antibodies or fragments thereof which specifically bind SEQ ID NO: 2, does not reasonably provide enablement for antibodies or fragments thereof which specifically bind to a substantially pure or recombinant 499E9 polypeptide exhibiting 100% sequence identity over a length of at least 12 contiguous amino acids to SEQ ID NO: 2, or to a fusion protein comprising 499E9 sequence SEQ ID NO: 2 as recited in claim 10 (a) and (c). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or the invention commensurate in scope with these claims.

There is insufficient guidance and direction as to make and use 499E9-specific antibodies wherein the antibodies and antigen binding fragments thereof bind a 499E9 polypeptide exhibiting 100% sequence identity over a length of least 12 contiguous amino acids of SEQ ID NO: 2 or a fusion protein comprising 499E9 sequence".

The genus encompasses antibodies that can specifically bind 499E9 polypeptides wherein such 499E9 polypeptides have numerous differences in amino acid sequences at positions other than the length of 12 contiguous amino acids exhibiting 100% identity to SEQ ID NO: 2, including numerous differences in linear and conformational epitopes; and further encompasses antibodies which are coupled with an unlimited number of polypeptides as a fusion protein.

However, the present specification fails to provide sufficient disclosure of such 499E9 polypeptides that maintain the structural and functional properties of the 499E9 polypeptide set forth in SEQ ID NO: 2 wherein a stretch of 12 contiguous amino acids are 100% identical to SEQ ID NO: 2 and the other amino acids can vary. The specification does not provide sufficient guidance as to which of the amino acids may be changed while 499E9 structural or functional activity and specificity is retained. Further, the specification fails to provide guidance as to the unlimited number of polypeptides which can be fusion partners for SEQ ID NO: 2.

Coleman et al. (Research in Immunology, 1994; 145(1): 33-36) teach single amino acid changes in an antigen can effectively abolish antibody antigen binding. Abaza et al. (Journal of Protein Chemistry, Vol. 11, No. 5, 1992, pages 433-444) teaches single amino acid substitutions outside the antigenic site on a protein effect antibody binding. Futher, Lederman et al. (Molecular Immunology 28: 1171-1181, 1991) disclose that a single amino acid substitution in a common allele ablates binding of a monoclonal antibody (see entire document). Additionally, Li et al. (PNAS 77: 3211-3214, 1980) disclose that dissociation of immunoreactivity from other biological activities when constructing analogs (see entire document).

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Because of this lack of guidance, the extended experimentation that would be required to determine which modifications would be acceptable to retain occluding structural and functional activity, and the fact that the relationship between the sequence of a protein/peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable (e.g. see Ngo et al.; in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al., (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495.), it would require an undue amount of experimentation for one of skill in the art to arrive at the other 499E9 polypeptides encompassed by the claimed invention.

The scope of the claimed 499E9-specific antibodies is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of 499E9 polypeptides broadly encompassed by the claimed invention as recited in claims 10 (a) and (c). Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's or peptide's amino acid sequence, and, in turn, nucleic acid sequence, and still retain similar biological activity or structural specificity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the protein's structure relates to its function. However, the problem of predicting protein structure from mere sequence data of a limited number of proteins/nucleic acids and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein and finally what changes can be tolerated with respect thereto is extremely complex and well outside the realm of routine experimentation.

Thus, applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use of the claimed 499E9-specific antibodies in manner reasonably correlated with the scope of the claims broadly including a broad number of structural changes encompassed by the genus 499E9 as recited in claims 10 (a) and (c). The scope of the claims must bear a reasonable correlation with the scope of enablement. See In re Fisher, 166 USPQ 19 24 (CCPA 1970). Without such guidance, the changes which can be made in the 499E9 encoding nucleic acids and amino acids and still maintain biological activity or structural specificity of 499E9 is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

11. Claim 10 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of SEQ ID NO: 2 which comprises mouse 499E9; however, applicant is not in possession of any antibody against any 499E9 with 100% identity over a length of at least 12 contiguous amino acids to SEQ ID NO: 2, or any fusion protein comprising any species of SEQ ID NO: 2. Consequently, conception in either case cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. The sequences themselves are required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993).

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A description of a genus of polypeptide sequences may be achieved by means of a recitation of a representative number of antibodies which specifically bind any 499E9 with 100% identity over a length of at least 12 contiguous amino acids to SEQ ID NO: 2, or any fusion protein comprising any species of SEQ ID NO: 2, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.) Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Megan Jamroz, whose telephone number is (703) 308-8365. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Margaret (Megan) Jamroz, Ph.D.  
Patent Examiner  
Technology Center 1600  
January 24, 2002

  
CHRISTINA Y. CHAN  
SUPERVISORY PATENT EXAMINER  
GROUP 1800 1644

## Notice to Comply

Application No.

09/671,658

Examiner

Margaret E Jamroz

Applicant(s)

GORMAN ET AL.

Art Unit

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### NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

- ☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).
- ☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).
- ☒ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).
- ☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."
- ☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).
- ☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable form of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).
- ☐ 7. Other:

#### Applicant Must Provide:

- ☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".
- ☐ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.
- ☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216

For CRF Submission Help, call (703) 308-4212

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